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Long Term Outcomes of On-Pump CABG versus Off-Pump CABG

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Abstract

Objective: Assess the long-term outcomes including mortality, revascularization and myocardial infarction events to determine whether off-pump CABG is more effective for patients compared to on-pump CABG procedures.

Methods: Studies were found using PubMed with the search term, "on and off pump CABG" which yielded 1736 studies. After assessing for records within 5 years the search was narrowed to 370 articles and then down to 353 because some articles were not available in full-text. Our search was then divided into first looking at randomized control trials and meta-analysis availability from the 353 articles meeting our criteria. After narrowing our search for only randomized control trials, we were left with 47 articles. We lastly went back to the 353 articles and narrowed that search to only available meta-analysis which gave us 27 options. The final studies were chosen based on their relation to our clinical question.

Results: Studies show that there are no significant differences in the number of events sustained (or occurring) after both the off-pump CABG and on-pump CABG procedures. This was evident by results that varied between the three studies in which all percentages were close in number of events per population.

Conclusion: In regard to deciding whether to perform on-pump CABG or off-pump CABG, the physician and patient need to make a joint decision based on the patient's comorbidities and the physician's experience as a surgeon. There is not conclusive evidence that one approach is more effective than the other.

Introduction

Atherosclerotic plaque buildup in coronary arteries leads to approximately 400,000 patients across the United States undergoing an invasive procedure called a coronary artery bypass graft (CABG) each year.[1] CABGs remain the most common cardiac surgery in the United States and the standard of care for patients that suffer from left main coronary artery or 3-vessel coronary artery disease.[2] However, there are two approaches to performing the surgery, one which includes a cardiopulmonary bypass pump and the other procedure which is performed off the cardiopulmonary bypass pump. Regardless of the approach, the goal of the surgery is to bypass a blockage in a coronary vessel by using other vessels that have been harvested from another location within the body including internal mammary arteries, radial arteries and saphenous veins. The procedure is effective in its five-year outcomes, however it is unclear whether the benefits of off-pump coronary artery bypass graft are more effective than on-pump artery bypass graft. Among patients that meet criteria for a coronary artery bypass procedure, does the on-pump CABG procedure as compared to performing the CABG off-pump improve outcomes (mortality, revascularization, and myocardial infarction)?

On-Pump Procedure

On-pump coronary artery bypass is the more historical of the two procedures. However, it involves a lot of personnel and machinery to perform it correctly and efficiently. Included in the team needed to complete the surgery is a cardiothoracic surgeon, cardiothoracic physician assistant, anesthesiologist, perfusion technologist and the OR nurses. There are two components of cardiopulmonary bypass which consist of the pump and the oxygenator. In the on-pump procedure, patients are anesthetized using a neuromuscular blockage agent, anesthetic agent and heparin (IV dosed with 300-400 mg/kg of heparin) prior to performing a sternotomy in order to expose the epicardium/myocardium.[3] Next, the surgeon implants the cardiopulmonary bypass tubes into the right atrium with the distal cannula in the inferior vena cava. The aorta is then cannulated distal to the aortic clamp, with a goal of bypassing the heart and lungs once the heart is stopped for the procedure.[4] During this time, the patient's heart is put into a mild hypothermic state at approximately 34°C to prevent brain and vital organ tissue injury.[5]

At this point the heart is subsequently stopped using a potassium solution in addition to the hypothermia and the pump starts to pull the deoxygenated blood from the right atrium and takes it to the oxygenator. Inevitably, during oxygenation, oxygen bubbles are introduced to the blood which are filtered out prior to leaving the oxygenator. Lastly, the pump pushes the oxygenated blood from the oxygenator to the aorta in order to perfuse the body.[3] Upon completing the procedure, the temperature of the patient must be returned to 37°C at a rate of ≤0.5°C/min which could take 60-90 minutes.[6]

Once the bypass is set up, the CABG procedure is initiated by first harvesting the vessels needed to bypass the blockage(s). These vessels include the internal mammary artery, saphenous vein and radial artery depending on how many coronary vessels need to be bypassed. The arteries and/or veins are first sewed to a slit made in the aorta which will be the primary source of blood to that part of the heart. Lastly, the opposite end of the harvested vessel will be attached to a slit made in the blocked coronary vessel distal to the blockage, thus making a patent bypass. Prior to closing the patient, the surgeon will ensure patency and blood flow to the myocardium through the new vessels. The heart is capable of starting on its own; however, defibrillators are occasionally used along with temporary pacemakers.[7]

Off-Pump Procedure

Many of the preparatory steps of the off-pump coronary artery bypass procedure are similar to the on-pump however, the repair of blockages of the coronary artery or arteries is completed while the heart continues to beat. This procedure is also referred to as OPCABG (Off Pump Coronary Artery Bypass Graft)and is different than the traditional on-pump surgery that requires the usage of a heart and lung bypass machine. Special devices are utilized to stabilize and partially immobilize the specific tissues of the heart that the surgeon is repairing.[8]

Not all candidates that need a CABG are eligible for the off-pump procedure. Individuals who are at high risk are believed to benefit more from an off-pump CABG instead of an on-pump. These individuals include people with advanced atherosclerosis of the aorta, kidney problems and chronic lung disease.[9] Other candidates who might be considered for an OPCAB include patients that are over the age of 60 with multiple diseased vessels, history of stroke, poor heart function or are immunosuppressed. Individuals who would not be considered for this procedure include patients that have enlarged hearts, valvular disease or blockages into the myocardium.[10]

As with any surgical procedure,there are potential risks and specific complications associated with the off-pump CABG that include but aren't limited to heart attack, stroke, bleeding, deep wound infection, arrhythmias or irregular heartbeats along with potential nerve damage. The OPCABG is thought to have a slightly lower risk of complications unless there are other risk factors such as diabetes, obesity, smoking or alcoholism.[10] The procedure is believed to provide benefits such as a lower stroke risk, neurocognitive dysfunction, organ dysfunction and atrial fibrillation.[8]

Clinical Question

Prior to starting the investigation for studies to examine, a PICO, a framework used to develop a clinical question to use in search engines when investigating a topic, was created and is found in table 1. We were able to interview local health professionals in cardiothoracic surgery and found that coronary artery bypass surgeries are the most common surgeries performed. The population was defined as being any patient that meets the criteria of the American College of Cardiology Foundation and American Heart Association guidelines for CABG which was developed in collaboration with American Association for Thoracic Surgery, Society of Cardiovascular Anesthesiologists, and Society for Thoracic Surgeons. Our goal was to compare the outcomes of off-pump CABG to the on-pump CABG by using selected outcomes which were based off the most reliable and recent studies found and their measured outcome congruency which were mortality, revascularization and myocardial infarction.

Table 1. PICO Framework Table

P	Population	Patients that meet criteria for a coronary artery bypass procedure
I	Intervention	On-Pump CABG
C	Comparison	Off-Pump CABG
O	Outcome	Revascularization, Mortality and Myocardial Infarction

Clinical Question:
Among patients that meet criteria for a coronary artery bypass procedure, does the on-pump CABG procedure as compared to performing the CABG off-pump improve outcomes (mortality, revascularization and myocardial infarction?

Methods

Our search started with Google Scholar and Pubmed by searching “on and off pump CABG”. Google scholar led us to all articles presented by Pubmed which had a total result of 1736 studies. There were no duplicates to remove. After assessing for records within 5 years, the search was narrowed to 370 articles and then down to 353 because of some articles not being available in full-text. Our search was then divided by first looking into randomized control trials and meta-analysis availability from the 353 articles meeting our criteria. After narrowing our search for only randomized control trials, we were left with 47 articles. We chose “Five-year outcomes after on-pump and off-pump coronary artery bypass” and “Five-Year Outcomes after Off-Pump or On-Pump Coronary-Artery Bypass Grafting” because they allowed us to assess outcomes for 30 days up to 5 years which was hypothesized to be helpful in determining long term outcomes of both procedures. We lastly went back to the 353 articles and narrowed that search to only available meta-analysis which gave us 27 options. We chose “Current evidence of coronary artery bypass grafting off-pump versus on-pump: a systematic review with meta-analysis of over 16,900 patients investigated in randomized controlled trials” because it had the most total patients and lined up with parameters found in the two randomized control trials we chose that included mortality, revascularization rates, and incidence of subsequent myocardial infarctions. A PRIMA flow diagram of our systematic review is depicted in figure 1.

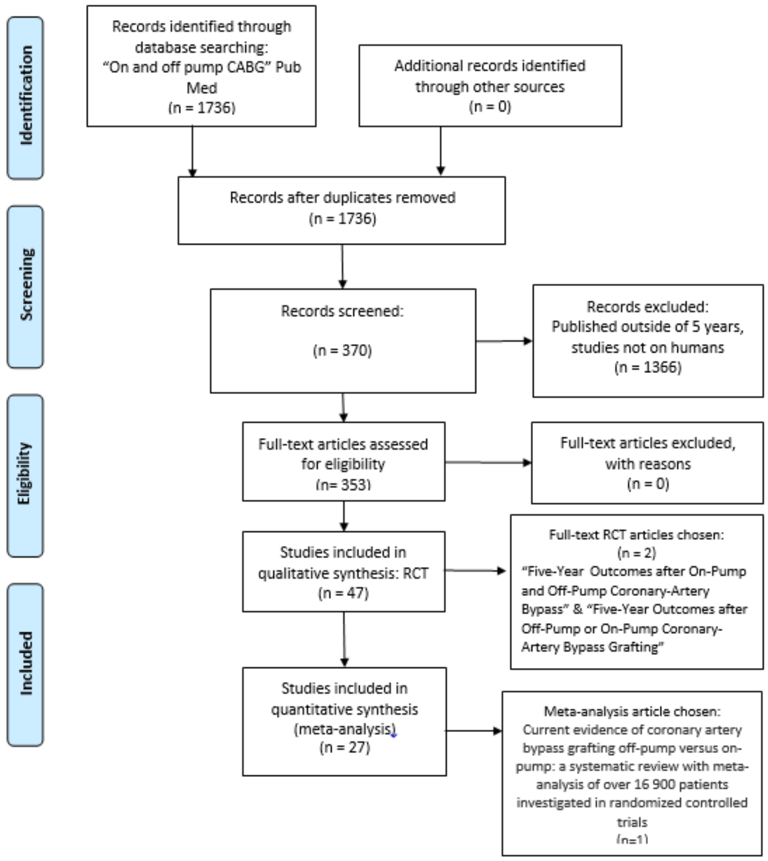

Figure 1. Prisma Flow Diagram [11]

Examined Studies

Study #1

Five-Year Outcomes after Off-Pump or On-Pump Coronary-Artery Bypass Grafting[12]

Objective: Evaluate the outcome of death, stroke, myocardial infarction, or renal failure between patients who underwent coronary-artery bypass grafting (CABG) performed with a beating heart technique (off-pump) and those who underwent CABG performed with cardiopulmonary bypass (on-pump) at 5 years.

Study design

This was a randomized controlled trial with blinded adjudication of outcomes where off-pump CABG and on-pump CABG were compared. Patients required an isolated CABG with median sternotomy along with one or more of the risk factors as seen in Table 2. A total of 4752 patients, from 79 various hospitals in 19 countries on four continents were randomly assigned to undergo a CABG procedure either on or off-pump. The surgeons have expertise in the specific assigned type of surgery to be performed with more than 2 years of experience after residency training and completion of more than

100 cases. If expertise in both techniques are met by a specific surgeon, they would be able to perform both type of procedures.

Follow-up with the patients was conducted in-person and on the telephone either with the patient or with their next of kin at 30 days and at 1 year after the procedure on a yearly basis until the end of the trial. If an outcome event is indicated the patient's physician was contacted to obtain source documentation concerning that specific event. The outcomes measured include death, nonfatal stroke, nonfatal myocardial infarction, nonfatal new renal failure requiring dialysis, and repeat coronary revascularization. These outcomes are divided into first coprimary which are being assessed at 30 days and 1 year and the secondary coprimary that are all identical to the first with the exception of the repeat coronary revascularization noted with an asterixis in Table 3.All deaths within the first 30 days were accounted for as cardiovascular deaths. Quality of life assessments were also evaluated with self-rated health scoring between 0 to 100%, with the higher score being a healthier status. Neurocognitive tests were also performed before the CABG, at discharge, 30 days, and at 1 year but not at the 5-year follow-up. Because no assessment was performed at 5 years this assessment was not included in this report.

The conduction of all analyses was completed according to the intention-to-treat principle, along with a time-to-event analysis with regression to report the long-term outcomes, after testing the assumption of proportional hazards. The first occurrence of the primary outcome is depicted with the Kaplan-Meier survival curves, and then the comparison between the two different treatment groups was compared with a log-rank test. The hazard ratio with 95% confidence intervals is used to demonstrate treatment effect derived from the Cox proportional-hazards model for the second coprimary outcome at 5 years. The two operative techniques are assessed within prespecified subgroups as seen in Table 3. If the patient had outcomes evaluated at 1 year without follow-up data, the info was excluded.

Table 2. Risk Factors determined by age

Age 70 years or more with 1 or more of the following risk factors:	**Age 60-69 years of age with at least 1 of the following risk factors or age 50-59 years with at least 2 risk factors:**
Peripheral arterial disease, cerebrovascular disease or carotid stenosis or 70% or more of the luminal diameter, or renal insufficiency.	Diabetes requiring treatment with an oral hypoglycemic agent or insulin, the need for urgent revascularization after an acute coronary syndrome, a left ventricular ejection fraction of less than 35%, or a history of smoking within 1 year before randomization.

Table 3. Coprimary outcomes
Outcome Events
Death Nonfatal stroke Nonfatal myocardial infarction Nonfatal new renal failure requiring dialysis Repeat coronary revascularization*

Table 4. Prespecified Subgroups
Subgroups
Diabetes Status Cerebrovascular disease status Left ventricular function Number of disease vessels Sex Age Body-mass index Region European System for Cardiac Operative Risk Evaluation (EuroScore)

Study Results

No significant differences were noted between the off-pump and on-pump CABG groups in the rate of composite outcome (23.1% and 23.6%, hazard ratio with off-pump CABG 0.98, 95% CI 0.87 to 1.10; P=0.72) or in the rates of the components of the outcome, including repeat coronary revascularization. Repeat revascularization was performed in 2.8% of the patients in the off-pump group and in 2.3% of the patients in the on-pump group (hazard ratio, 1.21; 95% CI, 0.85 to 1.73; P=0.29). No significant differences between groups in the quality-of-life measurements or the cost of the procedures was shown either. Based on this study, both procedures are equally effective and safe. To validate the consistency and validity of the results the treatment effects within the various subgroups were analyzed. It was determined that there were no significant interactions in the prespecified groups. The exception to this was the diabetes status group which showed an increase of secondary outcomes among the diabetics who underwent the off-pump CABG and a decrease in diabetics who had on-pump CABG. An apparent differential effect of treatment is therefore found among patients with diabetes.

Study Critique

No specific reasoning for the difference among the diabetes status subgroup was given and could not be validated with a significant interaction supported by other studies and additional information. Within the various subgroups the confounding variables were not treated any differently regardless of the intervention, with the exception being diabetics. There appeared to be an interaction between CABG type and diabetes status. Due to no significant findings between the treatment groups statistically or financially, a standard cost-effectiveness analysis was not completed. The specific cost of the supplies used for the procedures were not provided so a definitive cost analysis was unable to be completed. The quality-of-life and neurocognitive tests were optional for patients and not completed by everyone. An assessment at the end of the trial for neurocognitive status was unable to be completed.

There are many variabilities within this study including the variety of risk factors, and the country or continent which the procedure was completed. These individuals were randomly selected for each procedure, but some risk factors might have been more compatible with one procedure over the other resulting in different outcomes. The patients were randomized with blinded adjudication of outcomes. Other than the interventions the patients were all treated the same with follow-up and prior to interventions. The patients were aware of the intervention that would be occurring but were unaware as to why there were selected for that specific intervention. Follow-up data was provided for 98.8% of the patients and missing patients aren't addressed within the study.

Other things to be considered is that the quality-of-life measurement is subjective and may not accurately depict the improvement or decline in the quality-of-life for each patient. If no follow-up data was provided after outcomes evaluated at one year then this information would have been excluded from the study, potentially skewing the data from accurate evaluation and numbers with no follow-up data provided. Although these individuals don't want to be falsely accounted for either, if they had outcomes but no follow-up then the information is misleading.

The founding of this specific study was supported by the Canadian Institutes of Health Research. There was also grant support from Abbott Diagnostics, Boehringer Ingelheim, Covidien, Octapharma, Roche Diagnostics, and Stryker. Based on these grants there was likely a conflict of interest for the products and interventions. There were no other potential conflict of interests that were relevant or reported within the article.

Study #2

Five-Year Outcomes after On-Pump and Off-Pump Coronary-Artery Bypass[13]

Objective: To determine the 5-year clinical outcomes of patients included in the Veterans Affairs trial of on-pump versus off-pump CABG.

Study design

The original trial was a randomized, controlled, single-blinded trial that looked at the 1-year assessment of outcomes in CABG procedures. These same participants were used under the same trial methods to look then at the 5-year clinical outcomes. The mortalities that occurred within the last 5 years was assessed by using the data in the VA (Veteran Affairs) Vital Status Files along with the National Death Index to determine the cause of death. Chart reviews and databases like the VA National Patient Care Database, VA Patient Treatment File, VA-purchases care files, and Medicare Part A and B records were used to identify the nonfatal myocardial infarctions and repeat revascularization procedures.

Death from any cause, and MACE or major adverse cardiovascular events (a composite outcome of death from any cause, repeat revascularization [CABG or PCI], or nonfatal myocardial infarction) were the two primary outcomes monitored from the date of surgery to 5 years following the CABG. Comparisons between these two outcomes was then made between off-pump and on-pump treatments. Secondary outcomes included in the 5-year rates of death from cardiac causes, nonfatal myocardial infarction and repeat revascularization. Death from cardiac causes (rather than death from any cause), repeat revascularization or myocardial infarction was also assessed as additional secondary 5-year composite outcomes.

A committee consisting of cardiologists, cardiac surgeons, and the national nurse coordinator all were blinded to the treatment assignments of the patients and reviewed the trial outcomes. Initially assigned end-point categories made by the committee to medical charts included cause of death due to cardiac, non-cardiac or unknown etiologies. After these initial classifications were assigned, the committee compared these causes of death to the cause-of-death coding in the National Death Index and a final classification was then determined. If the committee didn't have sufficient data to determine a cause of death the National Death Index Coding cause of death was used.

Study Results

The patients used in the 5-year-follow-up study were monitored after randomization. At baseline the demographic characteristics and the risk characteristics did not significantly differ between the on-pump and off-pump treatment groups because the characteristics of patients at baseline were equal between the treatment types. The follow-up study used bivariate statistical comparisons for the hypotheses. This study was 99.4% men and the mean age was 62.7 years. Either two-vessel or three-vessel disease, hypertension, and normal or mildly depressed ejection fraction was present in most of the patients. This study represented the male veteran population who underwent CABG with coronary disease of mild-to-moderate severity and multiple coexisting conditions.

Table 5 shows the study outcome results within the 5 years following a CABG procedure. These outcomes were then evaluated in both primary and secondary outcomes. The primary outcome showed a significantly higher rate of 15.2% in the off-pump group compared to 11.9% in the on-pump group for the rate of death. The primary outcome MACE at 5 years also showed a significant difference between the off-pump group and the on-pump group at 31.0% and 27.1%, respectively (P=0.046). These numbers are reflected in Table 6. No statistical significance was found among any of the secondary outcomes between the on-pump and off-pump groups. Table 7 shows the difference between the treatment groups for secondary outcomes.

Table 5. Study Outcomes

Outcome	**Number of patients**
Deaths	299 deaths (13.6%) 128 cardiac-related death* (5.8%)
Nonfatal myocardial infarction	239 patients (10.8%)
Repeat revascularization	279 patients (12.6%)

Table 6. Primary Outcomes

Outcomes	**Off-pump**	**On-pump**
Death	15.2%	11.9%
Primary MACE outcome	31.0%	27.1%

Table 7. Secondary Outcomes

Outcomes	**Off- pump**	**On-pump**
Death from cardiac causes	6.3%	5.3%
Nonfatal myocardial infarction	12.1%	9.6%
Repeat revascularization	13.1%	11.9%

Study Critique

This study included patients within the Veterans Affairs trail which isolates a very select group of individuals. This group of patients had increased rates of hypertension, peripheral vascular disease and atrial fibrillation. The urgent status of these patients was also lower, along with lower rates of diabetes and female sex. Most of the participants in this study were men and don't accurately account for a significant number of females as a comparison. This study doesn't account for major cardiovascular events such as stroke rates post procedure.

Unfortunately, the care for veterans prior to, during and after service is not always the best which could lead to the higher rates of other comorbidities. Accounting for the overall health of these individuals although both group's risk characteristics were equal, they might have been poor prior to the procedure. With only looking at veteran individuals it's hard to make the same comparisons to non-veteran groups of individuals.

Study #3

Current Evidence of Coronary Artery Bypass Grafting Off-Pump Versus On-Pump: A systematic review with meta-analysis of over 16,900 patients investigated in randomized controlled trials[14]

Objective: To determine the current strength of evidence for or against off-pump and on-pump coronary artery bypass grafting (CABG) with regard to hard clinical end-points, graft patency and cost-effectiveness.

Study Design

This study was a meta-analysis that totaled 16,904 patients in a sum of 51 studies using the guidelines for Quality of Reporting of Meta-analysis. The electronic literature search was performed on March 5th, 2014 using Pubmed, EMBASE, and The Cochrane library. All 51 studies were published between February 1999 and March 2013. The 51 studies were chosen based off an extensive list of inclusion and exclusion criteria seen in table 8.

Among the 16,904 patients in this meta-analysis, 8,453 received an off-pump CABG through a median sternotomy. The age range of the patients in this study varied from 54.0-76.1 years of age. On average the patients receiving an off-pump CABG had ejection fractions that were 1.8% higher than the on-pump population. Our main focus for this review was to evaluate the clinical outcomes which were measured as mortality, repeat revascularization, myocardial infarction, cerebrovascular accidents, low cardiac output, renal dysfunction, length of hospital stay (cost) and "other clinical outcomes" such as transfusion and infection.

All the data including authorship, year of publication, type of publication, study design, length of follow-up, patient population, number of performed distal anastomosis, length of ventilation, ICU (Intensive Care Unit) and hospital stay, and desired clinical endpoints were extracted. Research quality assessment was performed by the investigators using the Jadad score and Down and Black checklist (measures methodological quality; High if score > 21) with disputes being resolved by consensus.

Statistical analysis was performed using the Review Manager Software and StatsDirect. The authors used I^2-statistics for heterogeneity between the studies that were included in the meta-analysis. The Mantel-Haenszel method was used between studies without heterogeneity and the DerSimonian and Laird random effects model was used when heterogeneity was present. The effect estimates of categorial data were calculated as weighted averages in the form of odds ratio and its 95% confidence interval. For continuous variables, the weighted mean differences (WMD) below 0 showed favoritism towards off-pump over on-pump CABG. Publication bias was also measured using the Egger's weighted regression statistic which was applied with a P-value <0.05. The subsequent studies showing significant publication bias were investigated by the authors by analyzing subgroups of the study to ensure high quality.

Table 8. Inclusion and Exclusion criteria for research studies included in the meta-analysis	
Inclusion	**Exclusion**
All studies published in full-text or abstract form were eligible for inclusion All randomized control trials comparing on-pump and off-pump CABG and reporting at least one event in one of the predefined clinical outcome parameters: - Surgical myocardial revascularization through a median sternotomy - Comparing off-pump CABG myocardial revascularization to on-pump CABG - At least one reported event on the incidence of desired postoperative clinical end-points a) Mortality b) Myocardial infarction/damage c) Cerebrovascular accident d) Repeat revascularization	Animal studies In vitro studies Prevention trials Editorials Letters Review articles or trials that reported other clinical outcomes Studies not including a proper control group Studies that did not report an event or a desired end-point Those that included the same patient population in more than one publication Those that only reported the protocol of an included trial

Study Results

Results can be found in table 9 which shows the parameters in which all of the studies investigated following on-pump versus off-pump CABGs. Each parameter varied in sample size because all of the 51 studies that were looked at did not measure all of the same parameters. The study found that mortality rates short-term (30 days) or long-term (1-7 years), myocardial infarctions and cerebrovascular accidents were no different between the two surgical approaches. However, off-pump CABG showed a 1.9-fold increase in risk of requiring a repeat revascularization with the first 30 days post-surgery. Additionally, cardiopulmonary bypass caused a 2-fold increase in low cardiac output, but when off-pump was performed, they saw a 45% risk reduction. Lastly, renal dysfunction risk was reduced by 2.1% with off-pump CABG. Length of stay in the ICU was changed with off-pump CABGs, showing a WMD -.36 days with a total hospital stay decrease shown by a WMD of -1.04 days. Off-pump CABG also showed a reduction of as a result of shorter duration of hospital stays, total costs were diminished by a WMD of -2,369 dollars. This could all be due to the reduction of the length of ventilation following off-pump CABG supported by a WMD of -3.50 hours.

Table 9. Analyzed clinical outcomes comparing on-pump versus off-pump CABG.

Dichotomous	**Sample size (*n*)**	**Prevalence % (*n*)**	**OPCAB % (*n*)**	**CABG % (*n*)**	**OR (95% CI)**	**χ^2-test (*P*-value)**
Death	16,718	2.0% (328)	1.8% (151)	2.1% (177)	0.86 (0.69–1.06)*	0.1606
Cardiac death	6,506	2.0% (130)	1.9% (63)	2.1% (67)	0.94 (0.66–1.32)**	0.7795
Myocardial infarction	12,496	4.7% (589)	4.6% (285)	4.9% (304)	0.93 (0.79–1.10)[†]	0.4450
Repeat revascularization	10,840	0.59% (64)	0.8% (42)	0.4% (22)	1.87 (1.13–3.11)[††]	0.0176
Cerebrovascular accident	15,562	1.5% (237)	1.3% (100)	1.8% (137)	0.74 (0.58–0.95)[‡]	0.0186
Low cardiac output	2,245	6.8% (153)	4.9% (56)	8.8% (97)	0.52 (0.37–0.73)[‡‡]	0.0003
Renal dysfunction	13,052	12.0% (1571)	11.0% (718)	13.1% (853)	0.79 (0.71–0.89)[§]	0.0003
Renal replacement	12,212	1.5% (179)	1.3% (78)	1.7% (101)	0.78 (0.58–1.04)[§§]	0.0945
Atrial fibrillation	10,709	21.8% (2339)	21.2% (1139)	22.5% (4232)	0.77 (0.59–1.01)•	0.1160
Infection	10,801	5.6% (600)	4.7% (255)	6.4% (345)	0.72 (0.60–0.85)••	<0.0001
Rethoracotomye	11,710	2.3% (268)	2.1% (121)	2.5% (147)	0.82 (0.64–1.04)[◊]	0.1099
Transfusion[a]	11,595	45.6% (5286)	40.4% (2344)	50.8% (2942)	0.60 (0.47–0.75)[◊◊]	<0.0001

Thirty-day follow-up. Summary of pooled effect estimates of all included trials reporting data of clinical outcomes off-pump coronary bypass (OPCAB) or coronary artery bypass surgery (CABG) with the use of the cardiopulmonary bypass. Effect estimates were calculated in the presence (I^2 > 50%) or absence of heterogeneity among trials by using either the random effects (DerSimonian–Laird) or fixed effects method (Mantel–Haenszel) as indicated.

CI: confidence interval; *n*: number of patients; OR: odds ratio with values less than 1 favoring OPCAB.
[a]Indicating recipients transfusion.
* Heterogeneity: I^2 = 0%, fixed effects (Mantel–Haenszel): overall effect *P* = 0. 1687.
** Heterogeneity: I^2 = 0%, fixed effects (Mantel–Haenszel): overall effect *P* = 0. 7825.
† Heterogeneity: I^2 = 0%, fixed effects (Mantel–Haenszel): overall effect *P* = 0. 4311.
†† Heterogeneity: I^2 = 46%, fixed effects (Mantel–Haenszel): overall effect *P* = 0. 0191.
‡ Heterogeneity: I^2 = 0%, fixed effects (Mantel–Haenszel): overall effect *P* = 0.0229.
‡‡ Heterogeneity: I^2 = 8%, fixed effects (Mantel–Haenszel): overall effect *P* = 0.0002.
§ Heterogeneity: I^2 = 0%, fixed effects (Mantel–Haenszel): overall effect *P* < 0.0001.
§§ Heterogeneity: I^2 = 0%, fixed effects (Mantel–Haenszel): overall effect *P* = 0.1024.
• Heterogeneity: I^2 = 79%, fixed effects (Mantel–Haenszel): overall effect *P* = 0.0594.
•• Heterogeneity: I^2 = 0%, fixed effects (Mantel–Haenszel): overall effect *P* < 0.0001.
◊ Heterogeneity: I^2 = 15%, fixed effects (Mantel–Haenszel): overall effect *P* = 0.1082.
◊◊ Heterogeneity: I^2 = 79%, fixed effects (Mantel–Haenszel): overall effect *P* < 0.0001.

Study Critique

The main goal of this meta-analysis was to determine the strength of evidence for or against off-pump CABG and on-pump CABG. 16,904 patients that were eligible for Coronary Artery Bypass Graft procedures were assessed through 51 different studies. The outcomes were evaluated using hard clinical end-points, graft patency, and cost-effectiveness. The investigators searched PubMed, EMBASE and The Cochrane Library independently using a predefined keywords list. All eligible studies for inclusion were published in full-text or abstract form. No language restrictions were enforced. Inclusion and exclusion criteria can be found in Table 8.

All randomized controlled trials comparing Off-Pump CABG and On-Pump CABG and reporting at least one event in one of the predefined clinical outcome parameters were identified and analyzed using the following a priori defined inclusion criteria: (i) surgical myocardial revascularization through a median sternotomy; (ii) studies comparing off-pump myocardial revascularization and on-pump surgery using CPB with cardioplegic arrest and (iii) at least one reported event on the incidence of desired postoperative clinical end-points: (a) mortality, (b) myocardial infarction or damage, (c) CVA and (d) repeat revascularization. The end-point definitions used by the primary authors (i.e. myocardial infarction) were accepted. The methodological quality of the included studies was assessed by two independent investigators (Antje-Christin Deppeand Wasim Arbash) using the Jadad Score [total score from 0 (poor) to 5 (excellent)] for RCT, and the Downs and Black Checklist [total score from 0 (poor) to 29 (excellent)] for both RCT and observational trials. Disagreements regarding the scores were resolved by consensus.

Regarding our desired parameters of revascularization, mortality and myocardial infarction, there was mild heterogenicity between studies in revascularization and mortality measurements. While the effect estimate of in-hospital mortality was associated with a higher grade of heterogeneity (I^2 = 46%), the follow-up data for repeat revascularization were less heterogeneous (I^2 = 19%). The investigators did not deem these numbers as significant heterogeneity, so a fixed-effect model was applied in the analyses. Data between studies measuring incidents of myocardial infarctions showed no heterogenicity. Authors did not elicit any conflicts of interest.

The authors concluded that both strategies are suitable for CABG procedures. The choice of procedure should be individualized for each patient according to associated comorbidities, life expectancy and the surgeon's training. The p-values vary depending on the outcome. In regards to our three main outcomes, the p-values were high for myocardial infarction (p= 0.4311) and mortality (p=0.1606). As a result, you cannot reject the null hypothesis that there is no difference between on-pump and off pump CABG resulting in myocardial infarction and mortality. Lastly, the null hypothesis of no difference between on vs off-pump CABG resulting in repeat revascularization can be rejected due to low p-value (p=0.0176).[14]

The meta-analysis was informational because it has a large number of patients receiving on and off-pump CABG which were compared. The advantage to pulling 51 studies together was that the authors could acquire info about many different outcomes to gain evidence as to which procedure is better. The study did not just limit itself to physical outcomes in determining which approach is most beneficial to the patient. By including both physical parameters and non-physical parameters, the authors portrayed they were investigating for the patient and not just for research purposes.

The numbers were portrayed in a chart (table 8) that was easy to read however the numbers within the description were somewhat cryptic. I would have liked the results section to be more informational about what numbers were considered significant especially when the number of patients being examined is so large. The revascularization results showed too much heterogeneity to include in our final results (I^2= 45%). Additionally, it might have been easier to report studies that used the same outcomes because the number of patients varied depending on outcome used.

A strong limitation to the study was the large number of trials reporting very small sample groups that included small amounts of events on clinical end-points. It is therefore unknown if the incidence of clinical end-points were underestimated. This study was also limited by the patient selection bias of the individual trials by including only healthy patients or excluded patients at risk who might benefit the most (low left ventricular ejection fraction, peripheral arterial disease, diabetes, renal dysfunction and senescence). Lastly, the experience of off-pump CABG surgeons was varied between studies.

Discussion

There is a mixture of conclusions between studies. The first study showed no significant difference between the on-pump and off-pump treatment groups including the quality of life. The second study, discovered an increase in the rate of death among the off-pump patients along with an increase of MACE outcomes including deaths from any cause, repeat revascularization and nonfatal myocardial infarctions. The secondary outcomes however showed no significant difference. The second study was composed of male veterans with comorbidities (hypertension, peripheral vascular disease, and atrial fibrillation) which may have led to increased negative outcomes following CABG. The meta-analysis, evaluating a larger scale of patients and populations within the different treatment groups showed no significant differences in myocardial infarction or cerebrovascular accidents following a CABG procedure. Some risk reductions were noted in the off-pump treatment group including a risk reduction in low cardiac output, renal dysfunction, length of stays in the ICU following intervention and the total cost.

By putting all of the study's results to the outcomes together, it was determined that 100 people would need to be treated with off-pump CABG to see an incidence of mortality as compared to on-pump CABG. Additionally, it was determined that 100 patients would need to be treated with on-pump CABG for a need of repeat revascularization as compared to off-pump CABG. It is important to note that the third study was omitted from this factor because of degree of heterogeneity between studies found in that outcome among the 51 studies. Lastly, It was determined that 500 patients would need to be treated with an off-pump CABG to have an occurrence of myocardial infarction as compared to on-pump CABG.

The second randomized control study had 2,203 patients enrolled that received both on-pump and off-pump CABGs. Within the primary outcomes this study revealed that 30 people needed to receive on-pump CABG for one less death to occur, 26 people needed to be treated with an on-pump CABG for 1 less MACE to occur. Death occurred in 168 patients out of 1,104 receiving the off-pump CABG (15.2%), while it occurred in 131 patients ouf of 1,099 receiving the on-pump CABG (11.9%). When subtracting the two, the result is an absolute risk reduction (ARR) of 0.033 (ARR= 0.0152-0.0119= 0.033). This results in 30 patients that need to be treated (NNT) with an on-pump CABG for one less death to occur (NNT= 1/0.033). There were 342 patients out of 1,104 that suffered from a major adverse cardiac event or MACE in the off-pump CABG group (31%) and 298 patients out of 1,099 also suffered a MACE within the on-pump CABG group (27.1%). When these two groups are subtracted from each other, the result is the absolute risk reduction (ARR) of 0.039 (ARR= 0.031-0.0271= 0.039). A total of 26 patients need to be treated (NNT) with an on-pump CABG for 1 less MACE to occur (NNT= 1/0.039).

Also within the second study there were secondary outcomes that showed that 100 people needed to be treated for 1 less death from cardiac causes, 40 people needed to be treated with an on-pump CABG for 1 less non-fatal myocardial infarction to occur and finally that 83 people needed to be treated with an on-pump CABG for 1 less repeat revascularization to be completed. A death from cardiac cause occurred within 70 patients out of 1,104 within the off-pump CABG group (6.3%) as well as 58 patients our of 1,099 within the on-pump CABG group (5.3%). When subtracting these two groups from each other, the result is the absolute risk reduction (ARR) of 0.01 (ARR= 0.063-0.053=0.01). The result is that 100 people need to be treated (NNT) with an on-pump CABG for 1 less death of cardiac cause to occur (NNT= 1/0.01=100). A non-myocardial infarction occurred in 134 patients out of 1,104 in the off-pump CABG group (12.1%) and in 105 patients out of the 1,099 in the on-pump CABG group (9.6%). When subtracting these two from one another, the result is the absolute risk reduction (ARR) of 0.025 (ARR= 0.0121-0.096=0.025). The result is that 40 people need to be treated (NNT) with an on-pump CABG for 1 less non-fatal MI to occur (NNT= 1/0.025=40). A repeat revascularization occurred in 145 patients out of 1,104 within the off-pump CABG (13.1%) and in 131 patients out of 1,099 in the on-pump CABG group (11.9%). When subtracting these two from one another, the result is the absolute risk reduction (ARR) of 0.012 (ARR= 0.0131-0.0119=0.012). The result is that 83 people need to be treated (NNT) with an on-pump CABG for 1 repeat revascularization to occur (NNT= 1/0.012=83).

In the meta-analysis (study number 3), 333 patients needed to receive off-pump CABG for one less death and one less myocardial infarction to occur. Myocardial Infarction occurred in 285 out 6,295 patients receiving off-pump CABG (4.5%) and 304 out 6,291 patients receiving on-pump CABG (4.8%). When subtracting the two, the result is an absolute risk reduction (ARR) of 0.003 (ARR= 0.048-0.045= 0.003). The result was 333 patients that need to be treated (NNT) with off-pump CABG for one less myocardial infarction to occur (NNT= 1/.003). Similarly, off-pump CABG resulted in 151 patient deaths out 8,363 patient procedures (1.8%) and 177 patient deaths out of 8,355 on-pump procedures (2.1%) that yielded an ARR of 0.003. The NNT was also 333 patients that needed to be treated with off-pump CABG to prevent one death. Repeat revascularization was needed in 42 off-pump patients out of 5,616 (0.7%) compared to 22 on-pump patients out of 5,625 (0.4%). The result was an ARR of 0.003 leading to 333 patients needing to be treated with on-pump CABG for one less repeat revascularization to occur.

Patients that require a coronary artery bypass graft often are experiencing other comorbidities and risk factors. There are numerous things to consider when attempting to account for the variability within these results. Comorbidities such as hypertension, renal failure and peripheral vascular disease are risk factors that may impact a patient's status as a candidate for each procedure. The severity of the coronary disease, demographic and risk characteristics were similar among the patients undergoing the studies. The consensus from these studies reveals no significance between the on-pump and off-pump CABG long term outcomes.

Conclusion

Coronary artery bypass graft is critical in the management of coronary artery blockages to sustain life. The decision to perform on-pump versus off-pump CABG depends on the patient and physician having strong communication about comorbidities, surgeon skillset, and risk analysis. Risks and benefits of each procedure need to be completely disclosed to the patient based off of the risk analysis performed by the surgeon. More research needs to be done on the long-term effects based on patient characteristics prior to surgery as well as cost effectiveness post operatively. Additionally, it is not possible at this time to determine which approach is more beneficial because not all surgeons are able to perform the off-pump CABG at the same skill level due to years of experience, mentosr, and number of opportunities to perform these surgeries. Each study however, has shown that on-pump and off-pump CABG procedures have their risks and benefits allowing for a current conclusion that one approach is not inferior to the other.

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